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09/761,581	01/18/2001	John C. Smith	P 0276523 PHM.70639/US	4675

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EXAMINER

SWITZER, JULIET CAROLINE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,581	SMITH ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6,8 and 11-24 is/are pending in the application.
- 4a) Of the above claim(s) 3-6 and 11-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-3 and 8 in the paper filed 12/20/02 with traverse is acknowledged. Applicant's further election of the single polymorphism at position 457 of SEQ ID NO: 1, with traverse in paper number 13 is also acknowledged. Further, applicant's addition of claims 11-24 is acknowledged. Claims 11-23 can be restricted into the following groups:

Group III, claims 1-3, 11, and 24 drawn to methods of diagnosis of a polymorphism and methods of linkage analysis, classified in class 435/6.

Group IV, claims 1-3 and 12-24 drawn to methods of diagnosis of a polymorphism and methods of bioinformatics analysis, classified in class 702/19.

The methods of elected group I and groups III and IV are unrelated because they are drawn to methods with separate goals utilizing distinct method steps. It is noted that the methods of inventions I, III, and IV all share claims 1-3 and 24 in common. To the extent that each of these claims utilizes the method of claims 1-3 and 24, these claims are related, but the groups are also patentably distinct since they are drawn to methods that have different goals, require different method steps and would utilize separate reagents. The methods of invention I have the goal of treating humans and require a step of administering a drug to a human in need of treatment. The methods of invention III are drawn to linkage analysis and would require the study of patient populations in order to determine a relationship between a particular phenotype and a polymorphism or between a locus and a polymorphism. The methods of invention IV are

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drawn to bioinformatic analysis and would require analysis of information to look for biologically relevant trends. Claims 1-3 and 24 will be examined with elected group I.

2. Claim 3 is withdrawn from prosecution because it does not contain the elected polymorphism.
3. Claims 11-23 are withdrawn from prosecution as being drawn to non-elected subject matter in view of applicant's election of group I. Claim 24, which encompasses the method of claim 1, will be examined with the elected group.
4. Applicant traverses the restriction requirement. Applicants point out that claim 1 covers a method of diagnosis involving determining the sequence at "one or more" of the four specified positions that if the restriction requirement is allowed to stand it will limit applicants to claiming methods for determining the sequence at only one of the positions. This is not persuasive, nor is it necessarily accurate. Claims which particularly require the examination of more than one polymorphic site were not presented. The claims, as presented and restricted, only **required** the determination of the sequence at a single polymorphic site. The current claim set includes claim 24 which requires the examination of all four listed polymorphic sites. This claim is not separated from the elected polymorphism, but this does not remove the fact that claims which require only one of the polymorphisms are still restricted one from another. The restriction requirement was based on the claim set as presented, not a hypothetical claim set. Thus, since the claims requires only the sequencing of a single position, and all four of the recited positions are independent and distinct from one another and the search and examination of all four separately would pose a significant burden to the examiner, the requirement that applicant select a single polymorphism for examination is proper. The requirement is therefore made FINAL.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, for example "Detection of polymorphisms in the human pyruvate dehydrogenase E1 β gene."

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 2, 8 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 8 are is indefinite over the recitation "determining the sequence of the nucleic acid of the human at one or more of positions..." because it is unclear how you determine a sequence at a single position of a nucleic acid. The word "sequence" implies the determination of the nucleotide present at more than one position of a nucleic acid, yet the claims set forth that the sequence is determined at one or more of the recited positions. It is not clear how a sequence can be determined at a particular position. Amendment of the claim to recite, for example, "determination of the nucleotide present at position 457 of SEQ ID NO: 1" would obviate this rejection. Claims 2 and 24 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

Claims 1 and 12 are further indefinite over the recitation "determining the status of the human by reference to polymorphism" because it is not clear what this step is requiring. It is not clear what it means to determine the status of a human "by reference to polymorphism." Claims

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2 and 24 are also indefinite for this reason because they depend from claim 1 but do not clarify the issue.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 8, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting and sequencing the human pyruvate dehydrogenase E1 β (PDH E1 β) gene and portions thereof, does not reasonably provide enablement for methods which are limited to the detection of a polymorphism at position 457 of SEQ ID NO: 1. Furthermore, the specification does not provide enablement for methods in which a polymorphism is diagnosed and then a PDH drug is administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

This rejection applies to the instant claims insofar as they might be interpreted as methods for the detection of the presence or absence of particular single nucleotide polymorphisms. It applies to claim 8 insofar as the claim implies that there would be a connection between the step of detection of the polymorphism and the administration of the PDH drug. Insofar as the instant claims read generally on methods for sequencing the human pyruvate dehydrogenase E1 β (PDH E1 β) gene, this rejection does not apply. The teachings of the specification (at, e.g., page 17-18) and of the prior art as exemplified by Huh *et al.* and Ho *et al.* disclose methods of detecting and sequencing the PDH E1 β gene and portions thereof. Such

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methods are encompassed by the instant claims as written, and a person skilled in the art could clearly practice methods of detecting and sequencing a known gene without further guidance. However, it is unpredictable as to whether one of skill in the art could use without undue experimentation methods requiring detection of the polymorphism at position 457 of SEQ ID NO: 1 or methods for treatment which comprise detection of the polymorphism at position 457 of SEQ ID NO: 1, which methods are also encompassed by the claims. Furthermore, it is unpredictable as to whether one of skill in the art could use without undue experimentation a method which requires the examination of four different single nucleotide polymorphisms in the PDH E1 β gene.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of four different polymorphic sites. A restriction requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 457 of SEQ ID NO: 1. This enablement rejection considers only this site in the claims that recite polymorphisms in the alternative. With regard to claim 24, many of the examples in this rejection are directed at the elected polymorphism, but it is to be understood that the rejection applies to claim 24 also which requires the examination of four different polymorphic sites.

The instant claims are drawn to methods for the diagnosis of a polymorphism in an PDH E1 β gene in a human. The methods comprise steps in which the particular nucleotide is detected at a particular position in different portions of the human PDH E1 β gene. Claim 8 further comprises a step in which a PDH drug is administered in an "effective amount."

The specification teaches that diabetes, asthma, obesity, sepsis and peripheral vascular disease are all diseases in which modulation of pyruvate dehydrogenase activity could be of therapeutic benefit (p. 1). Further, the specification provides four polymorphisms in the PDH E1 β gene. In particular, the specification teaches a polymorphic site at position 457 of SEQ ID NO: 1, located in within the coding portion of the PDH E1 β . The specification teaches that this polymorphism is an A \rightarrow G substitution that does not result in a change in the encoded polypeptide sequence (p. 5). The specification is silent with respect to the effect of this polymorphism on the biological activity of the PDH E1 β gene, or the effect of any of the other three recited polymorphisms on the biological activity of the gene. The specification does not disclose any relationship between the presence of this polymorphism a change in the activity or expression of the PDH E1 β or between the presence of a particular allele of this polymorphism and any particular disease state or physiological condition. Thus, there is no enabled use suggested for the methods for the detection of the polymorphism or for the methods of treatment, because there is no use given for the detected polymorphism, which is the essence of the invention.

The prior art teaches a number of polymorphisms or discrepancies between different published versions of the PDH E1 β gene. Ho *et al.* provide a number of such differences in their table 1, and Huh *et al.* also discuss a number of such differences at page 13323. However, the prior art is silent with regard to the effect that any of these polymorphisms have on the encoded polypeptide or their association with any observable phenotype.

There is also a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with

regard to the functionality of polymorphic sites in genomic DNA. After a screening assay identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the β -globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

The level of skill in the pertinent art is quite high, i.e. generally a PhD in biochemistry, but the unpredictability in the art is higher. While the instant specification has disclosed a number of different polymorphisms in the PDH E1 β gene, it remains highly unpredictable as to

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the biological significance of these polymorphisms, particularly the elected polymorphism which is within the coding region but causes no difference in the amino acid sequence of the encoded polypeptide. With respect to polymorphisms that do not cause changes in encoded polypeptides, the specification merely postulates, "Polymorphisms may also affect mRNA synthesis, maturation, transportation and stability. Polymorphisms which do not result in amino acid changes (silent polymorphisms) or which do not alter any known consensus sequences may nevertheless have a biological effect, for example by altering mRNA folding or stability (p. 3)." Thus, the claimed method directed towards the diagnosis of polymorphisms, or treatment of disease following diagnosis of polymorphisms, for enablement of the full scope, requires the knowledge of unpredictable and potentially non-existent associations between the instantly elected polymorphism and some phenotypic trait. Even if the elected polymorphism is in some way associated with some disease, it is difficult (if not impossible) to know or predict from the teachings of the specification which disease or how the polymorphism is associated. That is, it is unpredictable as to whether the presence of a particular allele the polymorphism would confer a higher or lower likelihood of having the disease. In this case, the possible uses for the claimed methods are undefined, beyond the suggestion that they can be used to detect a disease associated with the PDH E1 β gene prior to treatment with a PDH E1 β drug.

The amount of direction or guidance presented in the specification with regard to how to use the instant invention is minimal. The specification teaches at page 10 that "Individuals who carry particular allelic variants of the PDH E1 β gene may therefore exhibit differences in their ability to regulate protein biosynthesis under different physiological conditions and may display altered abilities to react to different diseases." However, since the effects of any given

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polymorphism on gene activity are highly unpredictable, it is impossible to predict from the teachings of the instant specification what identifications can be made using the instantly claimed methods. That is, the specification does not provide any guidance as to how the polymorphism at position 457 of SEQ ID NO: 1 would be associated with any pharmaceutical agent. The specification does not discuss whether this particular polymorphism will increase the likelihood of a positive or negative response to any drug. Furthermore, with regard to claim 8, which recites a method of treatment of a human in need of treatment with a PDH drug, the specification does not provide any guidance as to what disease is in fact associated with the presence or absence of the polymorphism at position 457 of SEQ ID NO: 1, other than the suggestion that these methods could be carried out for any number of the diverse group of diseases listed in the specification (diabetes, asthma, obesity, sepsis and peripheral vascular disease). The specification further fails to provide any guidance as to the appropriated PDH E1 β drug to be administered after the detection of the polymorphism, or the desired effect of administration of the drug (i.e. to up or down regulate the activity of the gene, and how either of these is to be accomplished). The specification provides no guidance or working examples that teach or demonstrate the ability to use the disclosed polymorphic site as a marker for any disease in particular, or for disease in general, or how to use the disclosed polymorphism to select a proper course of treatment of a disease.

The quantity of experimentation required to discover how to use the instant invention is very high. In order to use the claimed invention, one would have to establish a relationship between the polymorphism at nucleotide 457 of SEQ ID NO: 1 some physiological or disease state or some disease treatment method. Indeed, even to use the method of claim 1 to identify

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patients suited for particular pharmaceutical agents, one would need to know that the polymorphism at nucleotide 457 of SEQ ID NO: 1 was in some way associated with response to some pharmaceutical agent. In order to obtain the type of information necessary to practice the claimed invention, one would be required to undertake the screening of hundreds or thousands of patients as well as possible hundreds of diseases or pharmaceutical agents. Even if such experiments were undertaken, it would still be unpredictable as to whether any associations would be detected, in light of the unpredictability of such associations, as already discussed. Thus, while one could perform further research to determine whether applicant's method would be useful in disease detection and/or treatment, it is unknown as to what the outcome of such research might be and as to whether any quantity of experimentation would result in the identification of an association between the A/G polymorphism at position 457 and any disease or condition. Further, absent a teaching the A/G polymorphism at position 457 is not associated with such conditions, it is further unpredictable as to whether detection of the A/G polymorphism at position 457 would be useful in predicting, e.g., the absence or decreased likelihood of such conditions.

Furthermore, it is noted that the practice of the invention of claim 8 requires the administration of a PDH drug. The specification describes such a drug as being any drug which changes the level of PDH or changes the activity of PDH (p. 4), but the specification does not provide examples of such drugs. Thus, the practice of the claimed invention would first require the development of "PDH" drugs, then determining the patient population "in need of PDH drugs," and then still establishing the relationship between these PDH drugs and the polymorphism(s) set forth in the claims (if any were to exist). The specification does not

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disclose a relationship between treatment with these yet discovered drugs and the polymorphism at position 457 of SEQ ID NO: 1. The identification of a relationship between and the elected polymorphism would be highly unpredictable, requiring an extensive amount of research and experimentation.

Thus, in light of the nature of the invention, the state of the art, the high level of unpredictability in the art, the lack of direction or working examples in the specification, and the high quantity of experimentation that would be required to practice the claimed invention, it is concluded that undue experimentation would be required to use the instantly claimed invention. Thus, with respect to claims 1-2, and 24, although the specification certainly enables one to detect the presence of the polymorphism(s) (i.e. the "make" portion of 112 1st paragraph), it would require undue experimentation in order to determine how to use the methods of claims 1-2 and 24. It would also require undue experimentation to make and use the method of claim 8. Considering all of the factors discussed herein, it is concluded that it would require undue experimentation to determine the particular disease state that can be diagnosed and treated and thus to practice the claimed invention commensurate in scope with the present claims.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 8 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

It is noted that the instant claims each recite methods which comprise the detection of nucleotide sequences at one or more of four different polymorphic sites. A restriction

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requirement was set forth in which applicant was required to select a single polymorphic site for examination. Applicant selected the polymorphism at position 457 of SEQ ID NO: 1. This utility rejection considers only this site in claims 8.

The instant claims are drawn to methods for the diagnosis of a method for treatment of a human in need of treatment with a PDH drug in which the polymorphism is identified and then a drug is provided. Each of the methods comprise steps in which the particular nucleotide present is detected at a particular position in SEQ ID NO: 1.

The specification teaches that the PDH E1 β gene has been associated with a number of diseases and physiological states. Further, the specification provides four polymorphisms in the PDH E1 β gene. In particular, the specification teaches a polymorphic site at position 457 of SEQ ID NO: 1. The specification teaches at page 10 that "Individuals who carry particular allelic variants of the PDH E1 β gene may therefore exhibit differences in their ability to regulate protein biosynthesis under different physiological conditions and may display altered abilities to react to different diseases."

None of these asserted utilities meet the standard of being specific, substantial, and credible. Generally, these are utilities that can be assigned to a broad class of invention, that is any method for detecting a polymorphism, thus they are not specific. Furthermore, the utilities set forth are not considered to be substantial because further experimentation would be required to reasonably confirm that the disclosed polymorphism is in fact diagnostic or prognostic of disease or in fact associated with the suitability of a particular pharmaceutical agent. The specification merely postulates that such utilities exist, but in order to practice the claimed

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invention, further experimentation would be required to determine an association between the polymorphism and some physiological state or disease.

Claim 8 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The utility rejection has not been applied to claims 1-2 and 24 because these claims encompass an embodiment that would have utility, namely the sequencing of the PDH E1 β gene, which itself is known to be associated with physiological and disease states. If the claims are narrowed to exclude this embodiment, these claims may be included in the utility rejection.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1, 2, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al. (Gene, 1990, 86:297-302).

Ho et al. teach a method for the diagnosis of a polymorphism in an PDH E1 β gene in a human which comprises determining the sequence of the nucleic acid of the human at position 457 of SEQ ID NO: 1, and determining the status of the human by reference to polymorphism in the PDH E1 β gene (p. 298 and Table 1). Specifically, Ho et al. teach a method for sequencing the PDH E1 β gene (p. 398) and comparing the gene to other known sequences of the PDH E1 β

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gene in order to identify regions where the two genes differ. In table 1 of their disclosure, Ho *et al.* provide a listing of discrepancies between their sequence and another known sequence of the PDH E1 β gene. Ho *et al.* each an A \rightarrow G transition at codon 116, identical to the A \rightarrow G transition disclosed herein at position 457 of instant SEQ ID NO: 1 (compare the sequence disclosed as nucleotides 433-441 in Table 1 of Ho *et al.* to nucleotides 452-460 of instant SEQ ID NO: 1, they are identical). Ho *et al.* further teach a method wherein each of the positions 457, 1191, 1198, and 1342 are determined and the polymorphisms are diagnosed. Ho *et al.* teach an A \rightarrow C transition at position 1191 and a C \rightarrow T transition at position 1198 of instant SEQ ID NO: 1 (compare nucleotides 1168-1182 of Ho *et al.* to nucleotides 1196-1201 of instant SEQ ID NO: 1). Ho *et al.* teach a transition of C \rightarrow A at position 1342 of instant SEQ ID NO: 1 (compare nucleotides disclosed in table 1 of Ho *et al.* as nucleotides 1318-1326 to nucleotides 1337-1345 of instant SEQ ID NO: 1). Thus, the teachings of Ho *et al.* clearly anticipate the instantly rejected claims as they determine the nucleotides present at each of the recited positions and further identify the polymorphic sites between two different samples containing the PDH E1 β gene.

Conclusion

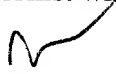
14. No claims are allowed.
15. It is further noted that Huh *et al.* (Journal of Biological Chemistry, Vol. 265, No. 22, 1990, pages 13320-13326 also teach an A \rightarrow G transition at position 457 of instant SEQ ID NO: 1. A rejection in view of this reference would have been duplicative.

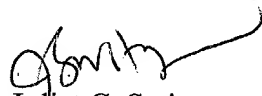
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16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703 308 1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.


JEFFREY FREDMAN
PRIMARY EXAMINER


Juliet C. Switzer
Patent Examiner
AU 1634

May 2, 2003